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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,145	ROBERTS, BRUCE L.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-10 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/1/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment and information disclosure statement were received and entered on 12/1/03.

Claims 13-20 were added as requested.

Applicants election with traverse of group 1, "PARC (SEQ ID NO:28)" is acknowledged. It is noted that SEQ ID NO:28 is decanucleotide and therefore cannot encode PARC which is an 89 amino acid polypeptide. Therefore Applicant's election of "PARC (SEQ ID NO:28)" is taken to address the requirement to elect a factor ("PARC") and an immunostimulatory tag from table 1 (SEQ ID NO:28). Traversal is on the grounds that the restriction requirement is not consistent with Office policy allowing examination of "up to 10 independent and distinct nucleotide sequences" in a single application (MPEP 803.04). This is not persuasive because the phrase "up to ten independent and distinct nucleotide sequences" allows for restriction to and examination of a single independent and distinct sequence, as has been required in this case. The requirement is deemed proper and is made FINAL. It is noted that the claims as amended no longer require any immunostimulatory tag listed in Table 1.

Claims 11 and 12 are withdrawn because they are drawn to non-elected subject matter. Applicant timely traversed the restriction requirement.

Claims 1-20 are pending and claims 1-10 and 13-20 are under consideration in this Office Action.

Drawings

No drawings are on file in the instant application.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. Because the specification fials to recite any priority claim (e.g. to PCT/US99/13800), the effective filing date of the application is considered to be 11/5/01,

Claim Interpretation

In the elected invention, claim 1 and dependents are drawn to a polynucleotide encoding an immunostimulatory factor that is differentially expressed in an antigen presenting cell, wherein the polynucleotide encodes PARC. At paragraph 228 of the specification teaches that:

> "SAGE analysis revealed for instance that the chemokines PARC and TARC that can recruit activated T cells are differentially expressed by monocyte-derived immature dendritic cells (prepared by culturing PBMC derived monocytes in GM-CSF and IL4)."

So, the specification teaches that PARC is an immunostimulatory factor that is differentially expressed in antigen presenting (dendritic) cells, and claim 1 may be narrowly interpreted as being drawn to a polynucleotide encoding PARC or a biologically active fragment thereof. However, the scope of these claims may be more broadly interpreted as embracing any polynucleotide that encodes any immunostimulatory factor that is differentially expressed in antigen presenting cells, wherein that polynucleotide must also encode PARC.

The scope of the term immunostimulatory factor is also interpreted as very broad. The specification does not limit the definition of this term but teaches at paragraphs 59, 67, and 69:

> The immunostimulatory factors of this invention include any polypeptide factors that modulate immune responses mediated by APC and corresponding T cells.
>
> In a separate embodiment of the invention, the immunostimulatory factor as claimed can be a co-stimulatory factor that is differentially expressed in monocyte-derived DCs. The costimulatory factor used herein will include at least a portion of the protein sufficient to allow binding to its costimulatory ligand expressed on corresponding T cell surface.
>
> Thus, according to one embodiment of the invention, the immunostimulatory factor as claimed can be a transcription factor regulating the gene expression of a co-stimulatory factor differentially expressed in monocyte-derived DCs.

As such, the term, "immunostimulatory factors" will be interpreted as embracing any polypeptide factor that modulates immune responses mediated by APCs, co-stimulatory factors, and transcription factors that stimulate expression of costimulatory factors.

The phrase "differentially expressed" is defined in a non-limiting manner in the context of a gene at paragraph 35 of the specification:

> "Differentially expressed" as applied to a gene, refers to the differential production of the mRNA transcribed from the gene or the protein product encoded by the gene. A differentially expressed gene may be overexpressed or underexpressed as compared to the expression level of a normal or control cell. In one aspect, it refers to a differential that is 3 times, preferably 5 times, or preferably 10 times higher or lower than the expression level detected in a control sample. The term "differentially expressed" also refers to nucleotide sequences in a cell or tissue which are expressed where silent in a control cell or not expressed where expressed in a control cell.

In the claims differentially expressed immunostimulatory factors are interpreted very broadly as embracing any immunostimulatory factor that is expressed in antigen presenting cells in a different amount, or with different kinetics, or under different conditions, than in other cells.

The term PARC is interpreted as referring to any polypeptide that comprises a recognized sequence of PARC that can act as a chemokine, including fusion proteins and fragments of PARC, particularly in view of the specification at paragraph 58 which discloses that the invention includes immunostimulatory polypeptides that are linked tumor antigens.

Claim Objections

Claims 17 and 18 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 7 is limited to a single polynucleotide, whereas claims 17 and 18 require at least 2 separate polynucleotides. Because claims 17 and 18 can comprise the entire scope of claim 7,

as well as material not embraced by claim 7, they are broader than claim 7 and do not further limit it.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4, 7-9, and 13-18 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-4, 7, 8, and 13-18 are drawn to various nucleic acids that occur in nature. For example, claim 1 is drawn to nucleic acids encoding PARC, which is differentially expressed in antigen presenting cells according to the specification at paragraph 228. Such nucleic acids are known to exist in nature because PARC is a chemokine expressed in human dendritic cells. The claims should be amended to show the hand of man in the invention, e.g. the claims could be amended to require "An isolated polynucleotide". Claim 4 is included in this rejection because a naturally-occurring cell is considered to be a gene delivery vehicle due to its transmission of chromosomes to daughter cells. Claim 7 is included in this rejection because the recited second polynucleotide that modulates expression of PARC can be a naturally-occurring chromosomal promoter. Claims 2, 3, 8, 13, and 16-19 are included in this rejection because PARC is encoded by human chromosome 17 (Guan et al (Genomics (1999 Mar 15) 56 (3) 296-302) see abstract), which also encodes the well known tumor antigen p53 (McBride et al (Proc. Nat. Acad. Sci. USA 83(1): 130-134) see abstract),

both of which are under the control of promoters. Pertinent to claims 14, 15, 17 and 18, cells comprising these chromosomes also comprise other chromosomes encoding tumor antigens under the control of promoters.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, and 13-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As discussed above, the claims may be broadly interpreted as embracing genus of polynucleotides encoding any immunostimulatory factor that is differentially expressed in an antigen presenting cell (APC), so long as that polynucleotide also encodes PARC.

The written description requirement can be met for genus claims through adequate description of a representative number of species. Species may be described by complete structure or reduction to practice, or they may be described by relevant identifying characteristic such as a known or disclosed correlation between structure

and function that is typical of the genus. See the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov).

In this case the claimed genus clearly includes all costimulatory molecules, cytokines, and chemokines as well as the transcription factors that are involved in their expression, see the specification at paragraphs 59, 67, and 69. The genus is also fairly interpreted as embracing any expressed polynucleotide that is in any way related to stimulating an immune response, so long as that polynucleotide is expressed in an antigen presenting cell in a way that is different in any way from the way it is expressed in any other cell. Note that this also includes polynucleotides that are not expressed in non-antigen presenting cells at all, so long as they are somehow involved in stimulating an immune response.

The specification discloses 2137 decanucleotides that are expressed differentially as parts of mRNAs in antigen presenting cells (see Table 1). The specification teaches that several hundred of these decanucleotides can be found in known mRNAs, whereas most of them are not found in any known mRNA. This is evidence that there is a wide variety of unknown mRNAs that are expressed differentially in antigen presenting cells. The instant claims are drawn to polynucleotides encoding "factors" that are differentially expressed in APCs, and so clearly embrace polynucleotides comprising complete mRNAs encoding such factors. So, the claims embrace a wide variety of complete mRNAs for which only 10 nucleotides of sequence are known. The claims do not limit the structure of the portion of the nucleic acid that encodes the factor in any way, the only limitation is function, i.e.

it must be expressed differentially in an APC. The courts have found that merely describing the functional characteristics of a protein encoded by a particular nucleic acid is insufficient to adequately describe the genus of nucleic acids encoding that protein. A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. See Oka, 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by a biological property, e.g., the cells in which it is differentially expressed, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. When an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated. Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The instant application does not provide a written description that would allow one of skill in the art to immediately envisage the specific structure for any of the mRNAs or proteins identified in Table 1 for which there is no currently known mRNA sequence. One of skill in the art would first have to isolated and determine that sequence. . *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in

possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed* (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-10, and 13-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoo (US Patent 5,891,432, issued 4/6/1999), as evidenced by Poznansky et al (US Patent 6,448,054).

Hoo teaches expression vectors encoding immunomodulatory molecules such as DC-CK1 (PARC) expressed as membrane-bound fusion proteins that are displayed on the surface of a cell, and cells comprising the vectors, as required by instant claims 1, 4, 5, 7, 9, 10, 19, and 20. See e.g. abstract, column 1, lines 10-24, column 12, lines 46-67, and column 21, lines 38-58. Relevant to claims 2, 14, 15, 17, and 18, exogenous disease-associated antigens, such as tumor antigens, can be expressed in the cells of the invention by using recombinant methods known in the art. See e.g. column 13, lines 45-58, and also paragraph bridging columns 12 and 13 for a discussion expression vectors known in the art. Alternatively, and pertinent to claims 3, 8, 13, and 16, the

expression vectors may encode a tumor antigen fused to the membrane-bound fusion protein comprising the immunomodulatory molecule, such that a nucleic acid encoding a fusion of PARC and a tumor antigen is within the bounds of the invention. See e.g. column 18, lines 1-32.

Thus Hoo anticipates the claims.

Note that DC-CK1 and PARC are known to be synonymous in the art. See e.g. US Patent 6,448,054 to Poznansky et al, paragraph 25 of detailed description.

Claims 1, 4, 5, and 7-10 are rejected under 35 U.S.C. 102 (b) as being anticipated by Hieshima et al (J. Immunol. 159: 1140-1149, 1997).

Hieshima teaches expression vectors encoding PARC and cells comprising the vectors. See Abstract, and Materials and Methods (e.g. page 1142, first full paragraph).

Thus Hieshima anticipates the claims.

Claims 1 and 6 are rejected under 35 U.S.C. 102 (b) as being anticipated by Brennan (US Patent 5,474,796, issued 12/12/95).

Brennan teaches an array of isolated oligonucleotides comprising every conceivable 10mer oligonucleotide sequence. See column 9, lines 48-55. Thus Brennan teaches every 10 nucleotide fragment of a nucleic acid encoding PARC. Absent evidence to the contrary, these fragments are biologically active, e.g. they could act as triplex-forming nucleic acids to modulate PARC gene expression.

Thus Brennan anticipates the claims

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 571-272-0564.

DAVE T. NGUYEN
PRIMARY EXAMINER

Richard Schnizer, Ph.D.